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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,115	AXON ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/04, 4/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II drawn to compound of Formula I wherein Z is CR^4 in the reply filed on 7/22/2005 is acknowledged. Election of species of compound 9 is also acknowledged. Claims 1-21 will be examined to the extent they embrace the elected subject matter.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The traversal is on the ground(s) that the triazine and elected pyrimidino are substantially interchangeable. This is not found persuasive. As noted in the previous office action, if applicants were to consider that these species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention. Applicants have done so.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-21 are pending.

Information Disclosure Statement

References cited in the Information Disclosure Statement filed on 1/20/2004 and 4/9/2004, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same limitation.

1. Recitation of " and pharmaceutically acceptable salts and prodrug forms thereof" in claim 1, renders this claim and its dependent claims 2-21 indefinite as it is not clear whether the claim is compound claim or composition claim with above said limitations. Note Markush recitation should be in alternate form and in singular.

2. In claim 1, recitation of the term "prodrug forms" is deemed as indefinite. Prodrugs in general and as noted in specification, are compounds, which undergo in vivo hydrolysis to parent active drugs. In that sense recitation of prodrug is acceptable. However, the definition of various variable R and X, groups include such groups, namely esters, amides, alkoxycarbonyl etc. and therefore it is not clear what is the difference between these variable groups and the prodrug groups. There is clear-cut ambiguity as to what is to be considered as prodrug and what is not. Applicants should note that if the variable groups are

prodrug, which are in general inactive but becomes active upon in vivo transformation, then the compound bearing the variable group would be deemed as inactive which is not what the claim recites.

Furthermore, the issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrugs" are molecules whose structure lie outside the subject matter of formula (I), but upon metabolism in the body are converted to active compounds falling within the structural scope of formula (I). The claim describes the function intended but provides no specific structural guidance to what constitutes a "prodrug". Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claim 1. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise. Applicants list the function that these prodrugs are to perform in the passage 029 but offer no structural guidance as to which derivatives are intended.

3. Recitation of "non-interfering substituent" in claim 1 renders this claim indefinite as it is not clear what is intended.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not

reasonably provide enablement for making prodrugs of the claimed compounds. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry - to use the invention. "The factors to be considered in making an enablement rejection have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, and produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism 'de novo, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active. Thus, determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

The definition concerning the prodrug is found in the passage 029. There is no working example of a prodrug of a compound the formula (I). The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the

human body. The state of the prodrug art is summarized by Wolff (Medicinal Chemistry). The table on the left side of page 976 outlines the research program to be undertaken to. find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modem Pharmaceutics) in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. I) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience. g) It is well established that "the scope of enablement varies inversely degree of unpredictability of the factors involved", 'and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula of claim I as well as the presently unknown list potential prodrug derivatives embraced by the word "prodrug".

Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the

application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claim 20 is rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating fibrosis of liver, does not reasonably provide enablement for treating any or all diseases or conditions mediated by TGFβ generically embraced in the claim language. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims..

The instant compounds are disclosed to have TGFβ inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all diseases including fibroproliferative diseases, treating collagen vascular disorders, treating eye diseases associated with a fbroproliferative condition, venting excessive scarring, treating neurological conditions and other conditions that are targets for TGFβ inhibitors and in preventing excessive scarring that elicits and accompanies restenosis following coronary angioplasty, cardiac fibrosis occurring after infarction and progressive heart failure, and in hypertensive vasculopathy, and keloid formation or hypertrophic scars occurring during the healing of wounds including surgical wounds and traumatic lacerations. Neurological conditions characterized by TGF/ production include CNS injury after traumatic and hypoxic insults, Alzheimer's disease, and Parkinson's disease.

Other conditions that are potential clinical targets for TGF/ inhibitors include myelofbrosis, tissue thickening resulting from radiation treatment, nasal polyposis, polyp surgery, liver cirrhosis, and osteoporosis. Diseases benefited by TGFP inhibition include cardiovascular diseases such as congestive heart failure, dilated cardiomyopathy, myocarditis, or vascular stenosis associated with atherosclerosis, angioplasty treatment, or surgical incisions or mechanical trauma, diseases associated with fibrosis and/or sclerosis, including glomerulonephritis of all etiologies, diabetic nephropathy, and all causes of renal interstitial fibrosis, including hypertension, complications of drug exposure, such as cyclosporin, HIV-associated nephropathy, transplant nephropathy, chronic urethral obstruction; hepatic diseases associated with excessive scarring and progressive sclerosis, including cirrhosis due to all etiologies, disorders of the biliary tree, and hepatic dysfunction attributable to infections such as hepatitis virus or parasites', syndromes associated with pulmonary fibrosis with consequential loss of gas exchange or ability to efficiently move air into and out of the lungs, including adult respiratory distress syndrome, idiopathic pulmonary fibrosis, or pulmonary fibrosis due to infectious or toxic agents such as smoke, chemicals, allergens, or autoimmune disease; all collagen vascular disorders of a chronic or persistent nature including progressive systemic sclerosis, polymyositis, scleroderma, dermatomyositis, fascists, or Raynaud's syndrome, or arthritic conditions such as rheumatoid arthritis; eye diseases associated with fbroproliferative states, including proliferative vitreoretinopathy of any etiology or fibrosis associated with ocular surgery such as retinal reattachment, cataract extraction, or drainage procedures of any kind; excessive or hypertrophic scar formation

in the dermis occurring during wound healing resulting âom trauma or surgical wounds, disorders of the gastrointestinal tract associated with chronic inflammation, such as Crolm's disease or ulcerative colitis or adhesion formation as a result of trauma or surgical wounds, polyposis or states post polyp surgery; chronic scarring of the peritoneum associated with endometriosis, ovarian disease, peritoneal dialysis, or surgical wounds; neurological conditions characterized by TGFP production or enhanced sensitivity to TGFP, including states post-traumatic or hypoxic injury, Alzheimer's disease, and Parkinson's disease; diseases of the joints involving scarring sufficient to impede mobility or produce pain, including states post- mechanical or surgical trauma, osteoarthritis and rheumatoid arthritis; and cancer.etc., for which applicants provide no competent evidence.

It appears that the applicants are asserting that the embraced compounds because of their mode action as TGFβ inhibitor that would be useful for all sorts of diseases and cancers. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as psoriasis and cancers, autoimmune diseases are very difficult to treat and despite the fact that there are many drugs, which can be used for "inflammatory condition".

The scope of the claims involves millions and millions of compounds of claim 1 as well as the thousand of diseases embraced by the terms proliferative disease, cancer, operating through TGF receptors.

Proliferative disease would include benign tumors, malignant tumors, polyps, lumps, lesions, other pre-cancerous conditions, psoriasis, leukemia, the hyper proliferation of the gastric epithelium caused by the Helicobacter pylori infection of ulcers.

Cancer is just an umbrella term. Tumors vary from those so benign that they are never treated to those so virulent that all present therapy is useless.

Inflammation is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, leukotrienes, cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

The "autoimmune diseases" are a process that can take place in virtually any part of the body. There is a vast range of forms that it can take,' causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There are hundreds such diseases, which have fundamentally different mechanisms and different underlying causes. Thus, the scope of claims is extremely broad.

No compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to

our present understanding of oncology. Cecil Textbook of Medicine states, "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Gressner et al. Front. Biosci. 7: 793-807 2002 (PubMed Abstract provided).

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence

or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating disorders/diseases that require TGFβ inhibitory activity.

2) The state of the prior art: Recent publication expressed that the TGFβ inhibition effects are unpredictable and are still exploratory. See Gressner et al. cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all condition of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all condition and the state of the art is that the effects of TGFβ inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace any or all proliferative diseases and cancers including those yet to be related to TGFβ.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-18, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Cai et al. WO 02/47690.

Cai et al. teaches several pyrimidine compounds, which include compounds, composition and the method of use claimed in the instant claims. See formula I on page 10 and note when A=C, given the same pyrimidine core, all variable groups overlap with those of the instant claims. Especially see formula II and III on page 11-12 which shows the desired pyrimidine compounds. See entire document for the details of the invention. See pages 13-34 for various species of pyrimidine compounds. See pages 139-152 for A Table of compounds. Especially see compound 73, 75, 46 and 20.

Claims 1-18, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Davies et al. WO 02/22607.

Davies et al. teaches several pyrimidine compounds bearing aminopyrazole, which include compounds, composition and the method of use claimed in the instant claims. See formula I on page 10 and note when ring A= choice a, given the same pyrimidine core, and G is phenyl, all variable groups overlap with those of the instant claims. See pages 6-45 for the details of the invention. See pages 46-103 for Table 1-6 for various species of pyrimidine compounds. Note several unfused pyrimidine compounds taught by Davies et al are also embraced in the instant claims.

Claims 1-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Kleemann et al. US 5,849,758.

Kleemann et al. teaches several pyrimidine compounds, which include compounds claimed in the instant claims. See formula I on column 1 and note when Z is N, given the same pyrimidine core, and A is aryl or heteroaryl, compounds taught by Kleemann et al include those of the instant claims. See column 1-3 for the details of the

invention. See column 3-5 for various species of pyrimidine compounds. See Table X for various compounds, which include instant compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cai et al., WO 02/47690.

Teachings of Cai et al. as discussed in the above 102 rejection is incorporated herein. As noted above, Cai et al teaches several pyrimidine compounds which include instant compounds.

Cai et al differ from instant claims in exemplifying only few compounds, which fall in the genus of instant compounds.

However, Cai et al. teaches the equivalency of those compounds exemplified with specific substituents with that generically recited on page 10-12 for Formula I-III See formula I-III and note the definition of various variable groups include several compounds. Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make pyrimidine compounds variously substituted with Ar_1, Ar_2, R_1, R_2 and R_3 as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1-18, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davies et al., WO 02/22607.

Teachings of Davies et al. as discussed in the above 102 rejection is incorporated herein. As noted above, Kleemann et al teaches several pyrimidine compounds which include instant compounds.

Davies et al, although exemplifying several compounds, which fall in the genus of instant compounds, does not fully exemplify all compounds embraced in the genus of

Formula I. However, Davies et al. teaches the equivalency of those compounds exemplified with specific substituents with that generically recited on pages 6-34 for Formula I. See formula I and note the definition of various variable groups include several compounds.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make variously substituted pyrimidine compounds as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kleemann et al., US 5,849,758.

Teachings of Kleemann et al. as discussed in the above 102 rejection is incorporated herein. As noted above, Kleemann et al teaches several pyrimidine compounds which include instant compounds.

Kleemann et al, although exemplifying several compounds, which fall in the genus of instant compounds, does not fully exemplify all compounds embraced in the genus of Formula I. However, Davies et al. teaches the equivalency of those compounds exemplified with specific substituents with that generically recited for formula I. See formula I and note the definition of various variable groups include several compounds. Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make variously substituted pyrimidine compounds as permitted by the reference and expect resulting compounds (instant

compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Acting Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

8/7/2005